REMARKS

This is filed in response to the Non-Final Office Action dated July 17, 2006, which rejects claims 1-4, 6-24 and objects claim 5.

Amendments to the Claims

Claim 1 has been amended to recite delivering a genetically altered chondrocyte used for expressing a therapeutic agent, to a target region having one or more cells associated with a disorder. The genetically altered chondrocyte expresses the therapeutic agent in such a way as to modify an environment surrounding the one or more cells. Additionally, the said environment is an atypical chondrocyte environment and the genetically altered chondrocyte does not become a structural component of the environment. Support for this amendment can be found throughout the specification, especially in paragraphs 007, 008, 010, 012, 035, and 062-081. Claim 5 has been cancelled as the subject matter of this claim is now incorporated into amended claim 1. Claim 6 to properly reflect its dependency on independent claim 1. Claims 2, 13, and 14 have been amended to overcome the Examiner's rejection and further clarify the claim language. No new matter has been added.

Claim Rejections under 35 USC § 102

Claims 1, 2, 5-14 and 17-24 are rejected by the Examiner under 35 U.S.C. 102(b)/(e) as being anticipated by U.S. Patent No. 6,413,511, (Gloriosos et. al., '511 reference). Applicants respectfully disagree with the Examiner.

Amended claim 1 recites delivering a genetically altered chondrocyte to a cell associated with a disorder. The genetically altered chondrocyte expresses a therapeutic agent which modifies an atypical chondrocyte environment surrounding the cell. However, the genetically altered chondrocyte does not become structurally functional in the environment surrounding the cell. The '511 reference does not teach or even suggest the use of genetically altered chondrocytes expressing a therapeutic agent to treat disorders in an environment atypical for chondrocytes. The '511 reference pertains to methods for introducing at least one DNA sequence expressing a protein or protein fragment of interest

into chondrocytes cultured in-vitro, and the delivery of the transfected chondrocytes to a damaged region of cartilage tissue, to alleviate articular cartilage defects. Further, the '511 reference teaches the use of genetically modified synovial cells to deliver therapeutic agents to diseased and/or damaged joints. In particular, this reference teaches the use of modified chondrocytes to repair cartilage defects by surgically implanting the chondrocytes and/or a chondrocyte-gel matrix at the site of repair. In fact, the Examiner acknowledges in the instant Office Action that the Glorioso reference primarily discloses the use of modified chondrocytes encoding a polypeptide of interest to deliver a therapeutic agent for treating joint diseases. Amended claim 1, clearly requires that the modified chondrocytes expressing a therapeutic agent, are specifically delivered to treat disease in an environment *atypical to chondrocytes*, (i.e., an organ or disease area where chondrocytes would not be present under normal physiological conditions). Further, claim 1 requires the modified chondrocytic cells to function only as vehicles for expressing and delivering the therapeutic agent required for alleviating the disease condition, without becoming an integral part (i.e., being structurally incorporated into the tissue) of the tissue or organ to which the chondrocytes are delivered. Thus claim 1 is neither anticipated nor rendered obvious by the prior art and represents patentable subject matter. Claims 2, 5-14 and 17-24 depend on claim 1 and therefore are allowable for at least the same reasons mentioned above for claim 1.

The Examiner further rejects claims 1, 2, 5-14 and 17-24 under 35 U.S.C. 102(e), and states that the above mentioned claims do not structurally distinguish the instant application over what was disclosed in the '511 patent. The Examiner further asserts that the '511 patent performs the same function as that described in the instant invention. Applicants respectfully disagree. The '511 patent, as stated above, teaches the use of genetically altered synovial or chondrocytic cells as vehicles to target the delivery of a therapeutic protein of interest to a diseased and/or damaged joint tissue. The '511 reference makes no mention of treating diseased tissues in areas other than in joints. However, amended claim 1, explicitly requires using the modified chondrocytes as delivery agents for therapeutics in an atypical chondrocyte environment. Thus claim 1, is distinct over the '511 reference, and Applicants request the Examiner to reconsider the rejection of claim 1 as well as all claims that depend from claim 1.

The Examiner also rejects claims 1, 2, 3, and 13-15 under 35 U.S.C. 102(b), as being anticipated by Bartholomew et. al., (Human Gene Therapy, 2001, Vol. 12, p 1527-1541). Applicants respectfully disagree.

The Bartholomew reference teaches the use of genetically altered mesenchymal stem cells (MSC) as cellular targets for gene therapy. Particularly, Bartholomew describes evaluating the functional capacity of transduced MSC's to secrete functional human Erythropoietin (hEPO) in-vivo, when delivered to mice either as an intramuscular injection or sub-cutaneously via the use of an inert immunoinsulatory device (IID). Barthlomew, does not teach or disclose, the use of genetically modified chondrocytes to deliver therapeutics for the in-vivo repair of a diseased tissue, and more importantly, Bartholomew does not disclose using modified chondrocytes for the in-vivo delivery of therapeutics in a diseased environment atypical to chondrocytes. The Examiner comments that Bartholomew reads on the claims of the instant application, since this reference discloses the in-vivo differentiation of the modified MSC's into chondrocytes. Applicants respectfully disagree with the Examiner. Bartholomew merely describes observing, post-implantation, an island of cartilage amongst the MSC's in at least one of the IID's that was used to deliver a high number of genetically modified MSC into mice . However, Bartholomew does not disclose the direct use of genetically modified chondrocytes to repair tissue damage in a region not associated with chondrocytes.

Further, it would not be possible for one of reasonable skill in the art to use the method taught in Bartholomew to build the Applicants claimed invention, as Bartholomew does not disclose all the limitations of claim 1, especially, the use of genetically modified chondrocytes as vehicles for the delivery of therapeutics to disease tissues in an atypical chondrocyte environment. Thus claims 1 and 13 are distinct over Bartholomew. The claims that depend from claims 1 and 13 are also distinct over the prior art for at least all the reasons mentioned above for claims 1 and 13.

Claim Rejections under 35 USC § 103(a)

Claims 4 and 16 are rejected by the Examiner under 35 U.S.C. 103(a) as being obvious over Bartholomew et. al., (Human Gene Therapy, 2001, Vol. 12, p 1527-1541).

Claims 4 and 16 recite a genetically altered chondrocyte that expresses an Erythropoietin mimetibody as the therapeutic agent. The Examiner states that the gene for EPO had already been characterized at the time of filing of the instant application. Thus, in the Examiner's opinion, it would have been obvious to one of ordinary skill in the art to develop a genetically altered chondrocyte that expresses the Erythropoietin mimetibody of the claimed invention. Applicants respectfully disagree.

First, Bartholomew reference teaches the use of genetically altered mesenchymal stem cells (MSC) as cellular targets for gene therapy. Particularly, Barthlomew describes evaluating the functional capacity of transduced MSC's to secrete functional human Erythropoietin (hEPO) in-vivo, when delivered to mice as an intra-muscular injection or delivered to baboons sub-cutaneously using an inert immunoinsulatory device (IID). Barthlomew, does not teach or disclose, the use of genetically modified chondrocytes for the in-vivo delivery of hEPO mimetibody as a therapeutic agent.

Second, the in vivo expression of functional mimetibodies is not a trivial task. It would require designing a vector to express the protein of interest in a form that would allow it to assert its desired therapeutic effect. This requires detailed knowledge of the principles of molecular biology, the biochemistry of the EPO protein, as well as genetics. Bartholomew does not disclose the DNA sequence of the gene encoding the EPO mimetibody, as this reference pertains to developing a method to use plueripotent cells, such as MSC, as promising cellular targets for gene therapy strategies. Thus, there would be no reason for one of ordinary skill in the art to combine Bartholomew's teachings with those for designing a vector for expression of a hEPO mimetibody in altered chondrocytes, and to build the Applicants claimed invention. Further, claims 4 and 16 depend on independent claims 1 and 13 which are patentable over Barthlomew for all the reasons mentioned above. Thus claims 4 and 16 are also patentable over Bartholomew.

Claim Rejections under 35 USC § 112

Claims 1-4 and 6-24 are rejected by the Examiner under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as invention.

Regarding claims 1 and 13, the term "a cell/region associated with a disorder" is regarded by the Examiner as rendering the claim indefinite because it is unclear what type of association the Applicants are referring to. Additionally, the term "structurally functional" renders the claims indefinite because it is unclear what type of function the Applicants are referring to. Applicants have amended claims 1 and 13 to overcome the Examiner's rejection and further clarify claim terms.

Accordingly, amended claim 1 recites a genetically altered chondrocyte expressing a therapeutic agent, when delivered to a *target region having one or more cells associated with a disorder,* expresses the therapeutic agent in such a way as to modify an environment surrounding the one or more cells. Furthermore, the said environment is an atypical chondrocyte environment, and the genetically altered chondrocytes *do not become a structural component of the environment.*

Similarly, amended claim 13 recites a genetically altered chondrocyte expressing a therapeutic agent *in an environment surrounding a cell associated with a disorder*, wherein the genetically altered chondrocyte is effective to be delivered to the environment and expresses the therapeutic agent to modify the environment surrounding the cell. Additionally, *the genetically altered chondrocyte does not become a structural component of the environment.*

The Examiner also states that claims 2 and 14 are indefinite because the term "an agonist or antagonist of an antibody" makes it unclear what type of agent the Applicant is referring to. Applicants have amended claims 2 and 14 to recite *"an antibody, a mimetibody...".* These amendments should clarify the claim terms and put the claims in condition for allowance. Applicants therefore request the Examiner to reconsider and withdraw the rejections of these claims.

CONCLUSION

Applicants believe that the presently pending claims are in immediate condition for allowance and allowance is therefore respectfully requested. However, should any issues remain, the Examiner is urged to telephone the undersigned Attorney for Applicant in the event that such a communication is deemed to expedite allowance of this application.

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Respectfully submitted,

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